

#### Molecular Modeling Approach to Ceramic/Polymer Composite for Biomedical Application

#### **THESIS**

Submitted to faculty of science-Ain Shams University in partial fulfillment for Degree of M.Sc. in Biophysics

Bv

#### **Amina Yousef Yousef Omar**

B.Sc. in Biophysics 2004

#### Supervised by

# Prof. Dr. El-Sayed Mahmoud El-Sayed

Prof. of Biophysics Physics Department Faculty of Science Ain Shams University

#### Prof. Dr. Wafaa Ismail Abdel-Fattah

Prof. of Bioceramics and Biocomposite Biomaterials Department National Research Centre

#### Dr. Medhat A. Abdel Khalek Ibrahim

Ass.Prof of spectroscopy
Physics Division
National Research Centre

Department of physics Faculty of Science Ain Shams University (2009)

#### **Approval Sheet**

# Molecular modeling approach to ceramic/polymer composite for biomedical application

By

#### **Amina Yousef Yousef Omar**

This thesis for master degree has been approved by

#### Prof. Dr. El-Sayed Mahmoud El-Sayed

Professor of Biophysics, Physics Department, Faculty of Science - Ain Shams University

#### Prof. Dr. Wafaa Ismail Abd El-Fattah

Professor of Bioceramics and Biocomposites, Biomaterials Departement - National Research Centre

#### Dr.Medhat A. Abdel Khalek Ibrahim

Ass.Prof of spectroscopy - Physics Division Nation al Research Centre



# النمذجه الجزيئيه لمتوالفات السيراميك/البوليمرات لتطبيقات الطبية

رسالة مقدمة من الطالبة

#### أمينه يوسف يوسف عمر

بكالوريس الفيزياء الحيوية ٢٠٠4

الى كلية العلوم جامعة عين شمس للحصول على درجة الماجستير في علوم الفيزياء الحيوية

#### تحت اشراف

ا.د. وفاع إسماعيل عبد الفتاح استاذ السير اميك الحيوى و المتوالفات الحيوية قسم المواد الحيوية المركز القومي للبحوث

#### ا.د. السيد محمود السيد استاذ الفيزياء الحيوية قسم الفيزياء

قسم الفيزياء كلية العلوم جامعة عين شمس

#### د.مدحت أحمد عبد الخالق ابراهيم

أستاذ مساعد قسم الطيف شعبة البحوث الفيزيقية المركز القومي للبحوث

> جامعة عين شمس كلية العلوم قسم الفيزياء (۲۰۰9)

#### رسالة ماجستير

اسم الطالب: أمينه يوسف يوسف عمر

عنوان الرسالة: النمذجه الجزيئيه لمتوالفات السيراميك/البوليمرات للتطبيقات الطبية

الدرجة العلمية: ماجستير

#### لجنة الاشراف:

د ا.د. / السيد محمود السيد استاذ الفيزياء الحيوية بقسم الفيزياء كلية العلوم جامعة عين شمس

2 ا.د. / وفاع إسماعيل عبد الفتاح استاذ السير اميك الحيوى و المتو الفات الحيوية المركز القومي للبحوث

3 د./مدحت أحمد عبد الخالق ابراهيم أستاذ مساعد قسم الطيف شعبة البحوث الفيزيقية بالمركز القومي للبحوث

لجنة التحكيم:

أجيزت الرسالة بتاريخ / / موافقة مجلس الجامعة / / تاريخ البحث / / الدراسات العليا ختم الاجازة / / موافقة مجلس الكلية / /

### صفحة العنوان

اسم الطالبة: أمينه يوسف يوسف عمر

الدرجة العلمية: الماجستير

القسم التابع له: الفيزياء

الكلية: العلوم

الجامعة: عين شمس

سنة التخرج: ٢٠٠4

سنة المنح: ٢٠٠٩

#### APPROVAL SHEET

Title of the M.Sc. Thesis

#### Molecular Modeling Approach to Ceramic/Polymer Composite for Biomedical Application

Name of the Candidate

#### **Amina Yousef Yousef Omar Supervisors** (Signature) Prof. Dr. El-Sayed Mahmoud El-Sayed (.....) Prof. of Biophysics **Physics Department** Faculty of science Ain Shams University. Prof.Dr.Wafa Ismail Abdel Fatah Prof. of Bioceramics and Biocomposite Biomaterials Department National Research Centre. Dr. Medhat A. Abdel Khalek Ibrahim (.....) Ass. Prof of spectroscopy **Physics Division** National Research Centre.



Name: Amina Yousef Yousef Omar

Degree: Master

**Department:** Physics — Biophysics Group

Faculty: Science

**University:** Ain Shams

Graduation Date: 2004 - Ain ShamsUniversity

**Registration Date:** 11/6/2007

**Grant Date: 2009** 

### **Contents**

# Table of Contents. List of figures. List of tables. List of Abbreviations.

#### Abstract.

No.	<u>Title</u>	<u>Page</u>
	Chapter 1: Introduction and literature review	1
1.1	Introduction	1
1.2	Molecular Modeling of composites	3
1.3	Composite biomaterials	13
1.3.1	Composite forms (methodology)	13
1.3.2	Characterization and mechanism of composite forms	16
1.3.3	Mechanical properties of chitosan/ hydroxyapatite composites	19
1.3.4	Biocompatibility of chitosan/ hydroxyapatite composites	20
1.3.5	Some recent applications of the composites	22
1.4	Aim of the Work	24
	Chapter 2: Theoretical Aspects	25
2.1	Molecular modeling	25
2.1.1	Molecular mechanics	26
2.1.2	Quantum mechanics	28
2.1.2.1	Semi-empirical method	29
2.1.2.2	Ab initio method	31
2.1.2.3	Density functional theory (DFT) methods	33
2.1.3	Some calculated parameters	38

2.2	Biomaterials	39
2.2.1	Ceramics	40
2.2.1.1	Calcium phosphate	41
2.2.2	Biopolymer	44
2.2.3	Composite materials	46
2.2.3.1	Bone as a composite	47
2.2.3.2	Chitosan/hydroxapatite composite	48
2.3	Methods of analysis and characterization	51
2.3.1	Structural analysis	51
2.3.1.1	Infrared analysis	51
2.3.1.2	X-ray diffraction (XRD)	51
2.3.2	Biophysical and Biochemical analysis	52
2.3.2.1	Spectrophotometer	52
2.3.3	Morphological features	52
2.3.3.1	Scanning Electron Microscopy (SEM)	52
	8	
	Chapter 3: Materials and methods	54
3.1	20 0	
	Chapter 3: Materials and methods	54
3.1	Chapter 3: Materials and methods  Molecular modeling	54 54
3.1 3.1.1	Chapter 3: Materials and methods  Molecular modeling Optimized geometry	54 54 55
3.1 3.1.1 3.1.2	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties	54 54 55 56
3.1 3.1.1 3.1.2 3.1.3	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties Vibrational spectra analysis	54 54 55 56 56
3.1 3.1.1 3.1.2 3.1.3 3.1.4	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties Vibrational spectra analysis QSAR properties	54 54 55 56 56 57
3.1 3.1.1 3.1.2 3.1.3 3.1.4 3.2	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties Vibrational spectra analysis QSAR properties Composite synthesis and characterizations	54 54 55 56 56 57 58
3.1 3.1.1 3.1.2 3.1.3 3.1.4 3.2 3.2.1	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties Vibrational spectra analysis QSAR properties Composite synthesis and characterizations Chemicals used	54 54 55 56 56 57 58
3.1 3.1.1 3.1.2 3.1.3 3.1.4 3.2 3.2.1 3.2.2	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties Vibrational spectra analysis QSAR properties Composite synthesis and characterizations Chemicals used Synthesis of chitosan/hydroxapatite composites	54 54 55 56 56 57 58 58
3.1 3.1.1 3.1.2 3.1.3 3.1.4 3.2 3.2.1 3.2.2 3.2.3	Chapter 3: Materials and methods  Molecular modeling Optimized geometry Electronic Properties Vibrational spectra analysis QSAR properties Composite synthesis and characterizations Chemicals used Synthesis of chitosan/hydroxapatite composites Characterization Fourier Transform Infra-Red Spectroscopy	54 54 55 56 56 57 58 58 58 60

3.2.4	Bioactivity	61
3.2.4.1	Simulated body fluid (SBF)	61
3.2.4.2	Biomimetic soaking	62
3.2.4.3	Soaking solution analysis	62
3.2.4.4	SBF uptake and SBF degradation tests	63
3.2.4.5	Scanning Electron Microscopy (SEM) and	64
3.2.4.3	Energy-dispersive X-ray spectroscopy (EDX)	04
	Chapter 4: Results and Discussion	65
4.1	Molecular Modeling of chitosan/hydroxapatite	66
4.1	interactions	00
4.1.1	Optimized structures	66
4.1.1.1	Chitosan optimized structure	66
4.1.1.2	Interaction of chitosan with hydroxyapatite	67
4.1.1.2. a	Chitosan with OH of Ca(OH) <sub>2</sub>	68
4.1.1.2. b	Chitosan with Ca ion	70
4.1.1.2. c	Chitosan with PO <sub>4</sub> <sup>3-</sup>	71
4.1.2	Calculated physical parameters	73
4.1.3	Chitosan/hydroxyapatite interaction as one	77
4.1.3	scheme	/ /
4.1.4	Calculated QSAR properties	79
4.1.5	Calculated vibrational spectra	83
4.1.5.1	Calculated spectra of chitosan	83
4.1.5.2	Calculated spectra for chitosan/hydroxyapatite	85
4.2	Results of chitosan/hydroxyapatite composites	90
4.2	and characterization	90
4.2.1	FT-IR Vibrational Spectra	90
4.2.1.1	Chitosan	90
4.2.1.2	Hydroxapatite	90
4.2.1.3	Chitosan/hydroxyapatite composite	91
4.2.2	X-ray diffraction (XRD)	94

4.2.3	Morphological characterization	96
4.2.4	Bioactivity and degradation	99
4.2.4.1	Soaking solution analysis	99
4.2.4.2	SBF uptake	101
4.2.4.3	SBF degradation (Weight loss)	102
4.2.4.4	Morphological characterization	104
4.3	Conclusion	107
	References	110
	الملخص العربي	

## **List of figures**

No.	Title	Page
figure 2.1	Model of hydroxyapatite (HA) crystal with atoms labeled according to element and symmetric type.	42
figure 2.2	Schematic diagram for both chitin and chitosan	45
figure 2.3	Structure of Bone	48
figure 3.1	Flow chart of preparation of chitosan/hydroxyapatite composites	59
figure 4.1	Calculated PM5 optimized chitosan of two units which is used in the present study.	67
figure 4.2	Schemes (1-4) of interactions (a) Scheme 1; OH of Ca(OH) <sub>2</sub> interacts with the N-H of chitosan unit 2. (b)Scheme 2; One OH of Ca(OH) <sub>2</sub> is coordinated with N-H of chitosan unit 2 while other ones is coordinated with the OH of chitosan unit 1. (c)Scheme 3; OH of Ca(OH) <sub>2</sub> is coordinated with N-H of both chitosan units.(d) Scheme 4; OH of Ca(OH) <sub>2</sub> is coordinated with N-H of chitosan unit 2 while the others ones are coordinates with oxygen (OH) of the same chitosan unit.	69
figure 4.3	Schemes (5-6) of interactions (a) Scheme 5; Ca is freely coordinated with N-H and OH of chitosan unit 2.(b) Scheme 6; Ca is freely coordinated with N-H and of chitosan unit 2,OH of unit 1 and to the oxygen of the linkage	70
figure 4.4	Schemes (7-8) of interactions (a)Scheme 7; P of PO <sub>4</sub> is coordinated with N-H and of chitosan unit 2, OH of unit 1 and to the oxygen of the	71

	linkage.(b)Scheme 8; O of PO <sub>4</sub> is coordinated with	
	N-H and of chitosan unit 2.	
	Scheme 9; Ca is freely coordinated with N-H and	
	of chitosan unit 2, OH of unit 1 and to the oxygen	
	of the linkage ,O of PO <sub>4</sub> is coordinated with N-H	
figure 4.5	and of chitosan unit 3. The length of interaction is	78
	indicated as 2.25 Å, 2.28 Å and 2.950 Å and 1.080	
	Å respectively.	
° 46		0.7
figure 4.6	Calculated PM5 vibrational spectrum for chitosan	87
	Calculated PM5 for chitosan and its interaction	
	schemes (a) vibrational spectra for scheme1-4 for OH interactions, (b) vibrational spectra for scheme	
	5-6 for OH interactions, (c) vibrational spectra for	
figure 4.7	scheme 7-8 for PO <sub>4</sub> interactions and (d) vibrational	88
	spectra for scheme 9 for Ca and PO <sub>4</sub> interactions	
	with chitosan	
	Calculated PM5 for all the studied schemes	
figure 4.8	indicating that all schemes are corresponding to	89
8	optimized structures	
	FTIR of chitosan /hydroxyapatite	
figure 4.9	composite(CS/HA ratios), (a)CS ,(b)90:10	93
	,(c)70:10 ,(d)50:50 ,(e)30:70 and (f)10:90	
	XRD of chitosan /hydroxyapatite	
figure 4.10	composite(CS/HA ratios), (a)10:90, (b)30:70	96
	SEM micrograph of chitosan /hydroxapatite	
figure 4.11	composite ratio	97

	50:50(a),(b),where(a)200x(b)500xand (c)EDX of	
	chitosan/hydroxapatite composite ratio 50:50	
	control in the control of the contro	
	SEM micrograph of chitosan /hydroxapatite composite ratios30:70(a),(b),where (a)1500x	
figure 4.12	(b)3500x and (c) EDX of chitosan/hydroxapatite	98
	composite ratio 30:70	
	Calcium and phosphorous concentration versus	
figure 4.13	time for chitosan /hydroxyapatite composite 50:50	100
	ratio	
	Calcium and phosphorous concentration versus	
figure 4.14	time for chitosan /hydroxyapatite composite 30:70	100
	ratio.	
	Percentage SBF uptakes of chitosan/hydroxyapatie	
figure 4.15	composite 50:50 and 30:70 ratios, during the time	102
E	of immersion in the SBF	
	Percentage of weight loss of	
	chitosan/hydroxyapatite composite 50:50 and	
figure 4.16	30:70 ratios, during the time of immersion in the	104
	SBF	
	SEM micrograph of chitosan /hydroxapatite	
	composite ratio 50:50(a),(b) after SBF, (a)1200 x,	
figure 4.17	(b)8000x and (c) EDX of chitosan/hydroxapatite	105
	composite ratio 50:50	
figure 4.18	SEM micrograph of chitosan /hydroxapatite	
	composite ratio 30:70 (a),(b) after SBF (a)120 x	106
	and (b)1000x(c) EDX of chitosan/hydroxapatite	100
	composite ratio 30:70	